Journal of Surgical Oncology 1999;70:190–193

Kimura's Disease: A Case Report and Literature Review

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Kimura's disease, which occurs endemically in the Far East and sporadically in the West, has so far eluded efforts to determine its exact pathogenesis. It presents as solitary or multiple benign swellings of the skin, has a predilection for the periauricular and scalp regions, and often is associated with regional lymphadenopathy. Morphologically, the lesions are characterized by proliferating blood vessels with rich eosinophilic infiltrate. Peripheral blood eosinophilia and raised serum IgE levels are signature features of the condition. The overall prognosis is good. When surgery is not possible, conservative treatment with either corticosteroids or radiation often can produce a favorable response. Complete surgical excision whenever feasible is the preferred treatment despite a high recurrence rate. Based on a recent case of Kimura's disease in a 55-year-old black woman, we discuss the pitfalls in the diagnosis of this chronic inflammatory disorder. *J. Surg. Oncol. 1999;70:190–193.*

KEY WORDS: Kimura's disease; angiolymphoid hyperplasia with eosinophilia; scalp lesions

INTRODUCTION

Kimura's disease is a rare benign entity of uncertain etiology. In 1948, Kimura et al. [1] described this condition as "an unusual granulation combined with hyperplastic changes of lymphatic tissue." Although the condition is prevalent in the Orient in an endemic form, only a small number of cases have been reported in the Western literature among blacks and Caucasians. Cases also have been reported in other parts of the world [2,3].

This chronic condition, which involves the head and neck area, often is accompanied by regional lymphadenopathy. It seldom resolves spontaneously, and malignant transformation has not been reported. Based on the case reported here, we have reevaluated Kimura's disease.

CASE REPORT

The patient, a 55-year-old woman with a history of bronchial asthma, insulin-dependent diabetes mellitus, and hypertension, presented to us in 1977 with multiple scalp lesions that had been growing insidiously for 25 years. She had experienced pain and intense itching with accelerated growth of these lesions over the last 2 months. Examination revealed 3 round, firm masses, each measuring up to 4.5 × 4 × 3 cm, covering an area approximately 15 cm in diameter on the frontoparietal portion of the scalp. The overlying skin was stretched, with impending ulceration. There was facial swelling and right jugulodigastric lymphadenopathy. Intraoral, nasopharyngeal, and systemic examinations were unremarkable.

The pertinent laboratory results were an eosinophil count of 45% and an erythrocyte sedimentation rate of 53 mm/hr. The serum IgE level was not measured. There was no proteinuria.

In view of the clinical presentation of these lesions, we considered the patient's condition to be benign. However, we could not exclude possibilities that a benign soft tissue mass had undergone malignant change, a low-grade malignancy such as dermatofibrosarcoma protuberans, or a chronic inflammatory condition. After biopsy, the masses were totally excised with clear margins.

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Accepted 12 December 1998

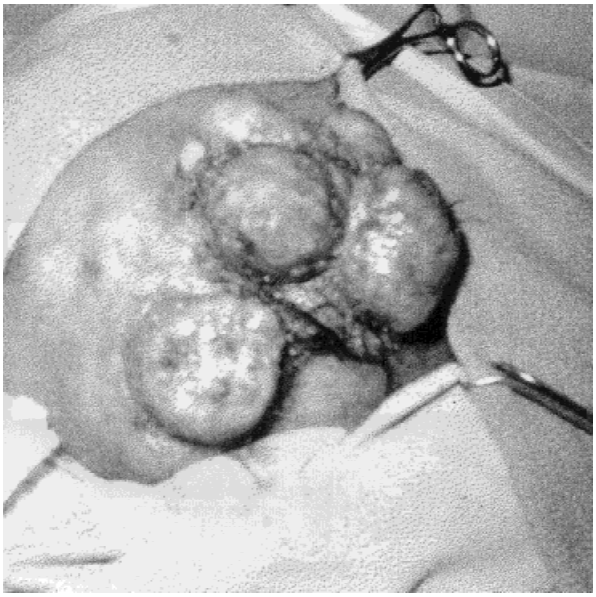

Fig. 1. Patient's scalp in 1981, disfigured by multiple tumor nodules.

The patient presented again in 1981 with an area of recurrence, 12 cm in diameter, and multiple scattered satellite nodules (Fig. 1). This was again widely excised with the resection extending to the pericranium. Closure of the skin defect was deferred. Two weeks later, secondary skin grafting was done to close the defect. The area has remained well healed with no further recurrence for 15 years. Her eosinophil count has remained normal and cervical lymphadenopathy has subsided. She continued to suffer from asthma and has developed renal failure for which she undergoes hemodialysis. The cause of renal failure has not been definitely ascertained.

PATHOLOGICAL FINDINGS

The initial scalp tumors, resected in 1977, and the recurrent lesions removed in 1981, exhibited similar features: multiple rubbery tumor nodules in the subcutaneous tissue measuring up to 5 cm in diameter. The cut surfaces were reddish-brown and mottled. Sections stained with hematoxylin-eosin (H&E) showed diffuse, dense infiltration of eosinophils and lymphoplasma cells. Occasional lymphoid nodules showed distinct germinal centers, intervening dense collagenized fibrosis, and marked vascular proliferation consisting of blood vessels of varying sizes lined by plump endothelial cells. The sections also contained scattered infiltrates of histiocytoid cells and mast cells (Figs. 2, 3).

Immunocytochemistry was performed on paraffin-embedded sections using antibodies (BioGenex, San Ramon, CA; and Dako, Carpinteria, CA) to T cells (CD3) and B cells (L26), as well as human macrophages (HAM 56); endothelial cells (factor VIII-related antigen); kappa and lambda light chains; IgG, IgM, IgA, and IgE heavy-chain immunoglobulins; the alpha-smooth muscle isoform of actin; proliferating cells (Ki-67); and mutant types of the p53 protein. There was a strongly positive reaction to factor VIII-related antigen on the prominent endothelial lining cells and a heterogeneous population of T and B cells with predominant IgM expression in the lymphoid nodules. There was diffuse infiltration of HAM-antibody-positive histiocytes, which were particularly pronounced around blood vessels. The majority of the vessels showed prominent perithelial cells, which were distinctly demonstrable by alpha-smooth muscle actin antibody [4] (Fig. 4). Interestingly, we observed mutant p53 protein in some endothelial cells. There was no significant immunoreaction to IgE in the lesions.

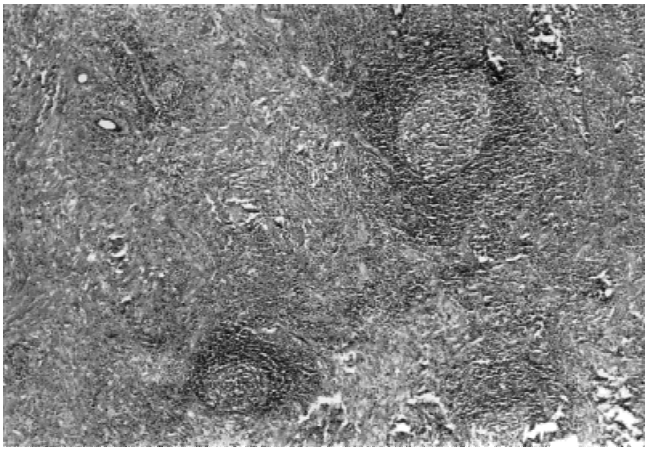

Fig. 2. Section showing intense infiltration of eosinophils. Also present are lymphoplasma cells with lymphoid follicles and marked proliferation of blood vessels (×40).

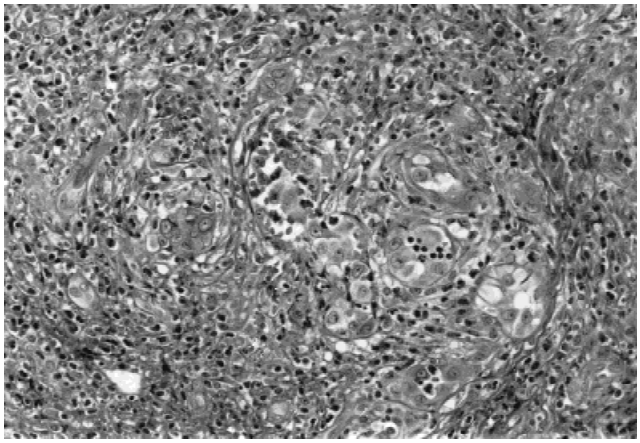

Fig. 3. Prominent endothelial cells of proliferating blood vessels (×400).

DISCUSSION

Since Kimura et al. [1] called attention to this disorder 50 years ago, its pathogenesis still has not been unrav-

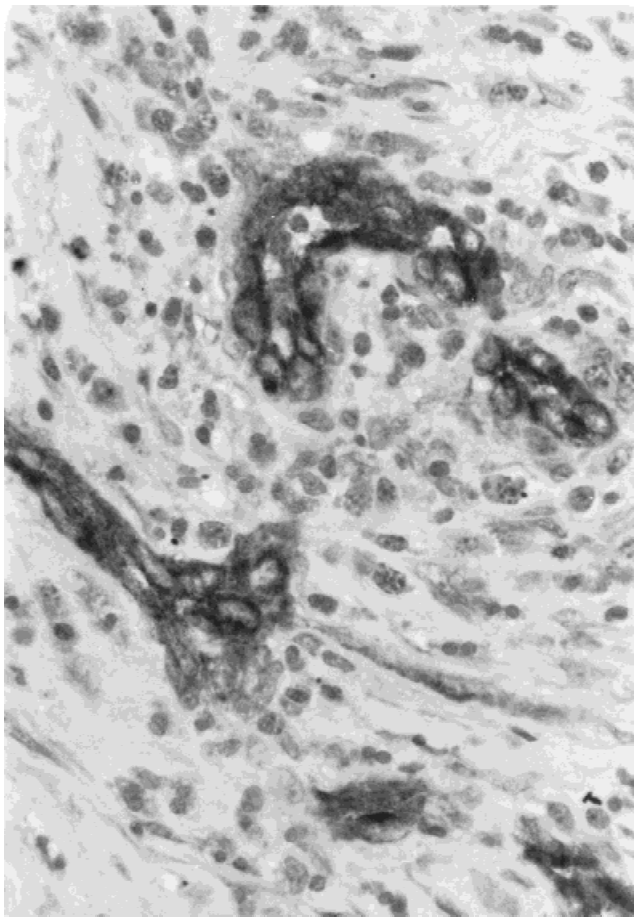

Fig. 4. Prominent perithelial cells demonstrated by immunocytochemistry using an alpha-smooth muscle isoform of actin (×400).

eled. The cause is believed to be either immune mediated or infective (parasitic or fungal), but no incontrovertible evidence exists on these points. The deposition of immune complexes seen on immunofluorescence lends credence to the notion that this condition occurs secondary to immunological injury [5]. It is likely that environmental or exogenous agents [6] may incite an immune response. Atopic allergy to *Candida albicans* has been detected [5].

Typically, Kimura's disease occurs in middle-aged individuals; it is more common in men than in women. Large, slowly growing masses in the head and neck region arise from subcutaneous tissues. Patients may have local pain and pruritus. Regional enlargement of lymph nodes [7], parotid, and submandibular salivary glands [8] can occur. Other possible sites of involvement are the paranasal sinuses, orbits, kidneys, and spermatic cord. Renal involvement from membranous glomerulonephritis can be manifested by concomitant proteinuria and nephrotic syndrome [9]. Bronchial asthma may coexist [10].

In the past, Kimura's disease and angiolymphoid hyperplasia with eosinophilia (ALHE) (also known as epithelioid hemangioma) often were considered to be the same disease. The fact that these designations were used interchangeably resulted in misconceptions about the disease process, as well as the classification and analysis of retrospective data. This controversy surrounding Kimura's disease and ALHE appears to have been settled [11,12]. Despite subtle clinical and histological similarities, Kimura's disease and ALHE now are considered to be separate entities.

ALHE is presently considered to be neoplastic in origin and represents the benign form of a broad sweep of vascular proliferations which includes epithelioid hemangioendothelioma (intermediate lesion) and epithelioid angiosarcoma (a malignant tumor). The lesions in ALHE are smaller and more superficially located than are those in Kimura's disease, and tend to be dermal or papular.

Because the histological features of Kimura's disease are not diagnostic per se, the differentiation of Kimura's disease from ALHE is still challenging. The endothelial cells in ALHE have a characteristic epithelioid or histiocytoid appearance. In addition, elevated eosinophil counts and raised serum IgE levels are strong pointers toward the diagnosis of Kimura's disease. The overall histological pattern may aid in diagnosis of Kimura's disease. In general, the involved lesions reveal unique features of vascular proliferation with plump endothelial cells and heavy eosinophilic infiltrate in a lymphoid background. Affected lymph nodes show a similar pattern and should be differentiated from a neoplastic process. The invariable features are follicular hyperplasia, eosinophilic infiltrate of the paracortex and sinuses, and many postcapillary venules. The variable features include sclerosis, deposits of proteinaceous material in the germinal centers, eosinophilic micro-abscesses, vascularization of germinal centers, and polykaryocytes of the Warthin-Finkeldey type. The immunohistochemical findings include IgE in germinal centers [5] and on the surface of non-degranulated mast cells.

Prior to biopsy, we did not consider the diagnosis of Kimura's disease in our patient because of its rarity in the West. Although the confluent vascular proliferation with prominent endothelial cells in our patient's scalp lesions mimicked hemangioendothelioma, the overall features of the tumor showed the distinctive histopathology of Kimura's disease. In addition, the immunocytochemistry of the lesions demonstrated prominent perithelial cells that were morphologically distinguishable from those in ALHE [4]. The demonstration of mutant p53 protein within epithelial cells was extremely interesting because this protein is usually not demonstrable in normal cells or benign conditions such as hemangioma. Moreover, Kimura's disease is considered to be a benign condition; no malignant transformation has ever been reported. Further study in a large number of cases may elucidate this observation.

The differential diagnosis includes conditions such as turban tumor (eccrine cylindroma) and dermatofibrosarcoma protuberans of the scalp. Other commonly encountered conditions with cervical swelling are Hodgkin disease, non-Hodgkin lymphoma, Mikulicz disease, and salivary gland neoplasms.

The limitations imposed in interpreting small cytological samples from fine-needle aspiration biopsy necessitate, when feasible, a more generous specimen obtained by incisional biopsy or excision. Fine-needle aspiration biopsy has a role in diagnosis of recurrent lesions and may obviate the need for an open biopsy [13].

The treatment of Kimura's disease is not well established. Surgery has a pivotal role in providing the diagnosis and for excising large, cosmetically unacceptable masses. Although surgery is effective and sometimes curative, recurrence rates are high [14].

The value of obtaining negative surgical margins in achieving sustained local control has not been studied. Complete excision is seldom possible. Corticosteroids may be tried prior to other treatment or following a recurrence. They generally usher in a significant response, but relapse is common after the discontinuation of treatment. Radiation is reserved for recalcitrant [15] and large lesions, or is used when surgery is not feasible or when an undesirable cosmetic or functional outcome is likely. The long-term effects of radiotherapy and its potential for causing dryness of mouth and permanent sequelae to the underlying brain have to be considered. Moreover, radiation and steroid therapy have unpredictable response rates. Cryotherapy, electrodesiccation, and laser fulguration have been tried with variable outcomes.

We present this case to increase awareness of this condition and to elucidate the pitfalls in its diagnosis. As noted, Kimura's disease and ALHE share common features, but are now considered to be separate entities. Because the course of Kimura's disease is indolent, treatment should be cosmetically sparing, preserving function while preventing recurrences and long-term sequelae. Based on the successful management of this case with wide surgical excision and skin grafting, we stress this mode of therapy.

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